

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/021641

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/17 A61K38/18 A61K38/19 A61K38/21 A61K45/00
A61K45/06 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ, COMPENDEX, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/66144 A (DARNOWSKI JAMES W ; CALABRESI PAUL (US); RHODE ISLAND HOSPITAL A LIFES) 13 September 2001 (2001-09-13) page 6, line 7 - line 32; claims 1,4 ----- -/--	1-3, 11, 12, 20-24, 32, 33, 44-46

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

24 January 2005

Date of mailing of the international search report

10.05.2005

Name and mailing address of the ISA

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Pilling, S

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>ALLEGRI G ET AL: "THE ANGIOGENESIS INHIBITOR THROMBOSPONDIN-1 PLUS IRINOTECAN SIGNIFICANTLY INHIBIT TUMOR GROWTH IN HUMAN COLON TUMOR BEARING NUDE MICE" PROCEEDINGS OF THE 91ST ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. SAN FRANCISCO, CA, APRIL 1 - 5, 2000, PROCEEDINGS OF THE ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, PHILADELPHIA, PA : AACR, US, vol. 41, March 2000 (2000-03), page 813, XP001019254 abstract</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>
X	<p>-----</p> <p>F.Y.F.L DE VOS: "A phase I dose escalating study of the angiogenesis inhibitor thrombospondin-1 mimetic (abt-510) in patients with advanced cancer" EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 38, November 2002 (2002-11), pages S78-S79, XP004403691 ISSN: 0959-8049 abstract</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>
X	<p>-----</p> <p>ARMSTRONG L C ET AL: "Thrombospondins 1 and 2 function as inhibitors of angiogenesis" MATRIX BIOLOGY, ELSEVIER, vol. 22, no. 1, March 2003 (2003-03), pages 63-71, XP002982095 ISSN: 0945-053X abstract</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>
X	<p>-----</p> <p>GUO N-H ET AL: "ANTIPROLIFERATIVE AND ANTITUMOR ACTIVITIES OF D-REVERSE PEPTIDES DERIVED FROM THE SECOND TYPE-1 REPEAT OF THROMBOSPONDIN-1" JOURNAL OF PEPTIDE RESEARCH, MUNKSGAARD INTERNATIONAL PUBLISHERS, COPENHAGEN, DK, vol. 50, no. 3, September 1997 (1997-09), pages 210-221, XP000696384 ISSN: 1397-002X abstract page 220, column 1, line 18 - line 24</p> <p>-----</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>STREIT MICHAEL ET AL: "Overexpression of thrombospondin-1 decreases angiogenesis and inhibits the growth of human cutaneous squamous cell carcinomas" AMERICAN JOURNAL OF PATHOLOGY, vol. 155, no. 2, August 1999 (1999-08), pages 441-452, XP001204804 ISSN: 0002-9440 abstract</p> <p>-----</p>	<p>1-3, 11, 12, 20-24, 32, 33, 44-46</p>
X	<p>REIHER FRANK K ET AL: "Inhibition of tumor growth by systemic treatment with thrombospondin-1 peptide mimetics" INTERNATIONAL JOURNAL OF CANCER, vol. 98, no. 5, 10 April 2002 (2002-04-10), pages 682-689, XP001204803 ISSN: 0020-7136 abstract</p> <p>-----</p>	<p>1-3, 11, 12, 20-24, 32, 33, 44-46</p>
X	<p>FEIGE J J: "The thrombospondins: Multimodular proteins with angiogenesis inhibiting effects" PATHOLOGIE BIOLOGIE, vol. 47, no. 4, April 1999 (1999-04), pages 339-344, XP009042623 ISSN: 0369-8114 abstract</p> <p>-----</p>	<p>1-3, 11, 12, 20-24, 32, 33, 44-46</p>
X	<p>LAWLER JACK: "Thrombospondin-1 as an endogenous inhibitor of angiogenesis and tumor growth" JOURNAL OF CELLULAR AND MOLECULAR MEDICINE, vol. 6, no. 1, January 2002 (2002-01), pages 1-12, XP009042620 ISSN: 1582-1838 abstract</p> <p>-----</p>	<p>1-3, 11, 12, 20-24, 32, 33, 44-46</p>
X	<p>HENKIN JACK ET AL: "Tumor inhibition by anti-angiogenic TSP-1 mimetic peptides" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 43, March 2002 (2002-03), page 180, XP001204805 & 93RD ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH; SAN FRANCISCO, CALIFORNIA, USA; APRIL 06-10, 2002 ISSN: 0197-016X abstract</p> <p>-----</p>	<p>1-3, 11, 12, 20-24, 32, 33, 44-46</p>
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>VAILHÉ BRUNO ET AL: "Thrombospondins as anti-angiogenic therapeutic agents." CURRENT PHARMACEUTICAL DESIGN. 2003, vol. 9, no. 7, 2003, pages 583-588, XP1204808 ISSN: 1381-6128 abstract</p> <p>-----</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>
X	<p>IRUELA-ARISPE M L ET AL: "INHIBITION OF ANGIOGENESIS BY THROMBOSPONDIN-1 IS MEDIATED BY 2 INDEPENDENT REGIONS WITHIN THE TYPE 1 REPEATS" CIRCULATION, AMERICAN HEART ASSOCIATION, DALLAS, TX, US, vol. 100, no. 13, 28 September 1999 (1999-09-28), pages 1423-1431, XP000923386 ISSN: 0009-7322 abstract page 1423, column 1, line 1 - column 2, line 2</p> <p>-----</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>
A	<p>US 5 639 725 A (FOLKMAN M JUDAH ET AL) 17 June 1997 (1997-06-17)</p> <p>column 2, line 63 - column 3, line 4</p> <p>-----</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>
A	<p>DATABASE WPI Section Ch, Week 200347 Derwent Publications Ltd., London, GB; Class B04, AN 2003-496683 XP002314426 & JP 2003 012541 A (FUJI PHARM IND CO LTD) 15 January 2003 (2003-01-15) abstract</p> <p>-----</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>
A	<p>US 6 576 632 B1 (AWAD M M A; BLAKE J F; GOLDSTEIN S W; KRAMER K W; LONGO K P; RAICHE K) 10 June 2003 (2003-06-10)</p> <p>column 1, line 9 - column 2, line 2</p> <p>-----</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>
A	<p>DATABASE WPI Section Ch, Week 200364 Derwent Publications Ltd., London, GB; Class B03, AN 2003-674472 XP002314427 & JP 2003 183249 A (RIKAGAKU KENKYUSHO) 3 July 2003 (2003-07-03) abstract</p> <p>-----</p>	<p>1-3,11, 12, 20-24, 32,33, 44-46</p>

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 02/076496 A (DUESBERY NICHOLAS S ; ANDEL INST VAN (US); WEBB CRAIG P (US); VANDE WO) 3 October 2002 (2002-10-03) abstract	1-3, 11, 12, 20-24, 32, 33, 44-46
A	WO 03/018748 A (KIMBERLY CLARK CO) 6 March 2003 (2003-03-06) abstract	1-3, 11, 12, 20-24, 32, 33, 44-46
A	WO 02/18380 A (HOFFMANN LA ROCHE) 7 March 2002 (2002-03-07) page 2, line 29 - line 32 page 40, line 16 - line 32	1-3, 11, 12, 20-24, 32, 33, 44-46
A	WO 02/18379 A (HOFFMANN LA ROCHE) 7 March 2002 (2002-03-07) page 3, line 1 - line 4 page 35, line 21 - page 36, line 3	1-3, 11, 12, 20-24, 32, 33, 44-46
A	WO 99/43311 A (JEFFERS MICHAEL E ; US HEALTH (US); WEBB CRAIG P (US); CZERWINSKI GREG) 2 September 1999 (1999-09-02) abstract	1-3, 11, 12, 20-24, 32, 33, 44-46
A	US 5 997 868 A (GOLDBERG ITZHAK D ET AL) 7 December 1999 (1999-12-07) column 3, line 40 - line 50	1-3, 11, 12, 20-24, 32, 33, 44-46
A	US 5 707 624 A (NICKOLOFF BRIAN J ET AL) 13 January 1998 (1998-01-13) abstract	1-3, 11, 12, 20-24, 32, 33, 44-46

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>ZHANG YU-WEN ET AL: "Hepatocyte growth factor/scatter factor mediates angiogenesis through positive VEGF and negative thrombospondin 1 regulation." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 100, no. 22, 28 October 2003 (2003-10-28), pages 12718-12723, XP001204754 ISSN: 0027-8424 the whole document</p> <p>-----</p>	<p>1-3, 11, 12, 20-24, 32, 33, 44-46</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/021641

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
3, 20, 21, 24, 44, 45, 46 and claims 1, 2, 11, 12, 22, 23, 32, 33 in part

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 3, 20, 21, 24, 44, 45, 46 and Claims 1,2, 11, 12, 22, 23, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising TSP-1 OR A TSP-1 FUNCTIONAL DERIVATIVE OR TSP-1
AGONIST OR TSP-1 MIMIC

2. claims: 1, 2, 11,12, 22, 23, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising ANGIOSTATIN

3. claims: 1, 2, 11,12, 22, 23, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising INTERFERON-ALPHA

4. claims: 1, 2, 11,12, 22, 23, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising INTERFERON-BETA

5. claims: 8, 29 and 1, 4 to 7, 11,12, 22 to 28, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising an ANTI-VEGF ANTIBODY

6. claims: 1, 4 to 7, 11,12, 22 to 28, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising an ANTI-VEGF RECEPTOR ANTIBODY

7. claims: 1, 4 to 7, 11, 12, 22 to 28, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a DECOY VEGF RECEPTOR

8. claims: 1, 4 to 7, 11, 12, 22 to 28, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a VEGF TRAP

9. claims: 1, 4 to 7, 11, 12, 22 to 28, 32, 33 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

composition/ methods for inhibiting tumour angiogenesis
comprising a SIRNA SPECIFIC FOR VEGF

10. claims: 1, 4 to 7, 11, 12, 22 to 28, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a SIRNA SPECIFIC FOR VEGF RECEPTOR

11. claims: 1, 4 to 7, 11, 12, 22 to 28, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a PEPTIDOMETIC INHIBITOR OF VEGF RECEPTOR
ACTIVATION

12. claims: 1, 9, 10, 11, 12, 22, 30, 31, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a NEUTRALIZING ANTIBODY SPECIFIC FOR HGF/SF

13. claims: 1, 9, 10, 11, 12, 22, 30, 31, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising NK4

14. claims: 1, 9, 10, 11, 12, 22, 30, 31, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a DECOY MET RECEPTOR OR FRAGMENT

15. claims: 1, 9, 10, 11, 12, 22, 30, 31, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a GENETICALLY ENGINEERED POLYPEPTIDES DERIVATIVE
OF MET WITH INHIBITORY ACTIVITY

16. claims: 1, 9, 10, 11, 12, 22, 30, 31, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a MET SPECIFIC SIRNA

17. claims: 1, 9, 10, 11, 12, 22, 30, 31, 32, 33 in part

composition/ methods for inhibiting tumour angiogenesis
comprising an INHIBITOR THE KINASE DOMAIN OF MET

18. claims: 1, 9, 10, 11, 12, 22, 30, 31, 32, 33 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

composition/methods for inhibiting tumour angiogenesis
comprising an INHIBITOR THAT TARGETS THE MULTI DOCKING SITE
OF MET OR ANOTHER AGENT THAT DECREASES HGF/SF OR MET
EXPRESSION

19. claims: 14, 35 and Claims 13, 34 and 40 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a MAPK pathway inhibitor that INCREASES THE
EXPRESSION OR ANTIANGIOGENIC ACTIVITY OF TSP-1

20. claims: 15, 36 and Claims 13, 34 and 40 in part

composition/ methods for inhibiting tumour angiogenesis
comprising a MAPK pathway inhibitor that DECREASES THE
EXPRESSION OR ANTIANGIOGENIC ACTIVITY OF VEGF

21. claims: 16 to 19, 37 to 39, 41, 42, 43 and Claims 13 and 34 in
part

composition/ methods for inhibiting tumour angiogenesis
comprising a MAPK pathway which is a MEK INHIBITOR

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/021641

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/021641

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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